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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,967	05/08/2001	Stuart A. Newman	51230-00601	1338

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EXAMINER	
YU, MISOOK	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,967	NEWMAN ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *31-36 and 43-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30, and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Misook Yu.

DETAILED ACTION

Election/Restrictions

On reconsideration groups II and III (corresponding claims 23-30) drawn to method of modifying RNA binding proteins and hnRNA binding proteins will be rejoined with the elected groups because claims 23-30 are duplicate of claims 39-42. Applicant's election with traverse of group 1 (claims 1-22, and 37-42) in Paper No. 12 is acknowledged. However, group IV-VI will not be joined with the elected group. Applicant traverses the restriction requirement (Paper No. 11) on the ground(s) that the inventions have not been shown to be independent and distinct and the examination of all groups would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups (the elected group and groups IV-VI) are distinct for the reasons set forth in Paper No. 11. See especially Paragraph #3. As to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Further, groups I-V do not belong to class/subclass specified in the previous Office Action; it was typographical error. They belong to class 435, subclass 375. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 31-36, 43-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 1-54 are pending and claims 1-30, and 37-42 are examined on merits.

Claim Objections

Claim 37 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1.

Claim 38 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 20.

Claim 38 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 20.

Claim 39 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 23.

Claim 40 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 25.

Claim 41 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 27.

Claim 32 is also objected to under 37 CFR 1.75 as being a substantial duplicate of claim 29.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 21, 22 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 21 and 22 depends from claim 2 drawn to method of modifying nucleotide binding enzyme comprising three active steps and claims 21 and 22 are drawn to determine step that is not part of active steps of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28, and 37-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "the polynucleotide sequences" line step b) but it is not clear what the metes and bounds are for the limitation.

Claims 1, 23, 27, and 37 recite the limitation "the activity" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 14 recites "the polynucleotide sequences are single-stranded" but it is not clear what the metes and bound are for the limitation. Does claim 14 further limits step a) or step b) of claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28, and 37-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of modifying activity of hnRNP A proteins, does not reasonably provide enablement for method of modifying activity of any other nucleotide binding proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are interpreted as drawn to method of modifying the activity of various nucleotide binding proteins by introducing **a nucleotide binding protein-specific substrate** (a polynucleotide sequence) into cells. The specification at pages 58-71 (Examples 1-3) and at Figure 5 teaches that hnRNP A1 activity could be modified by introducing hnRNP A1 protein binding polynucleotide sequence into cells. However, the specification does not teach method of modifying any other nucleotide binding protein, RNA binding protein, RNA alternate splicing regulatory protein, or hnRNP proteins. Blanchette et al (Apr 1, 1999,

The EMBO Journal, vol. 18, pages 1939-1952) at page 1939 (see the Introduction) teach that it has been difficult to sort out what nucleotide binding proteins, including RNA binding proteins, RNA alternate splicing regulatory proteins, and hnRNP proteins, bind to what kind of nucleotide sequence for pre-mRNA processing even with considerable effort by many brilliant different researchers in the field. Therefore, it appears that the art recognize figuring out what kinds of nucleotide sequence that a nucleotide binding protein binds to for pre-mRNA processing is unpredictable. Because of the limited guidance, lack of working examples, and unpredictability in the art, it is concluded that undue experimentation would be required to use the full scope of the invention as claimed.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 5 is interpreted as drawn to cell transfection method using a detergent since claims 2-5 appears to be drawn to transfection of cells with a polynucleotide. Neither the specification nor the art teaches transfection method using a detergent.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. Claim 13 is interpreted as drawn to method of modifying an activity of a nucleotide binding protein in cells by transfecting a RNA analog. Neither the specification nor the art teaches any RNA analog capable of modifying an activity of a nucleotide binding protein.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. Claim 19 is interpreted as drawn to method of modifying an activity of a nucleotide binding protein by binding of the protein to a transfected polynucleotide irreversibly. Neither specification nor the art teaches

any polynucleotide sequence that is bound to a nucleotide binding protein irreversibly, thereby modifying the activity of the protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 6, 11, 15-18, 20, 22-30, 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by **Blanchette et al** (Apr 1, 1999, The EMBO Journal, vol. 18, pages 1939-1952). The claims are interpreted as drawn to method of modifying an activity of nucleotide binding proteins (RNA binding proteins, RNA alternative splicing regulatory protein, hnRNA proteins, and hnRNP A1 proteins) by introducing a polynucleotide into cells (tissue culture cells). The binding of the transfected nucleotide sequence to the respective binding protein is inherent property of the proteins. Blanchette et al teach method of modifying activity (Exon skipping) of an hnRNP A1 protein in HeLa cells (human tissue culture cells) by transfecting a minigene (shown in Fig. 2 at page 1941) with the hnRNP binding sites and Northern analysis detection of the activity of the protein. See abstract, Fig.2, and paragraph bridging columns 1 and 2 of page 1940.

Claims 1, 3, 6-8, 10-12, 14-18, 20, 22, 37-40 are rejected under 35 U.S.C. 102(b) as being anticipated by **McNally et al** (Mar. 1999, Journal of Virology, vol. 73, pages 2385-93). The claims are interpreted as drawn to method of modifying an activity of nucleotide binding proteins (RNA binding proteins, RNA alternative splicing regulatory protein) by introducing a polynucleotide (RNA, a polynucleode comprising purified RNA, single-stranded, synthetic RNA) into cells (tissue culture cells, non-human cells, non-human mammalian cells). The binding of a nucleotide sequence of either transfected nucleotide sequence or sequence amplified from the transfected nucleotide sequence to the respective binding protein is inherent property of the respective proteins. McNally et

al teach a method of modifying snRNP proteins by transfecting a plasmid derived from Rous sarcoma virus. See abstract, Materials and Methods, page 2387, Figures 1-7.

Claims 1-4, 6, 14,15, 18, 20, 21, 37, 38, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by **Caceres et al** (1998, Genes Dev., vol. 12, pages 55-66). Claims 1-4, 6, 14,15, 18, 20, 21, 37, 38, and 39 are broadly drawn to method comprising only one active step of introducing a polynucleotide into tissue culture cells using known methods in the art (liposomes and electroporation). Step b) and c) is consequence of the active step a). Caceres et al teach transfection methods under Cell culture and transfection at page 63 left column, and the transfected polynucleotide modifying the activity of a nucleotide binding proteins such as RNA and DNA polymerases, many transcription factors and translation factors (all nucleotide binding proteins binding either double or single stranded RNA or DNA) is inherent consequences of the transfection. The consequence of the active step for example, claim 1 a) could be detected by phenotypic characteristics of cells. See the entire article, especially Figs. 1-6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchette et al (Apr 1, 1999, The EMBO Journal, vol. 18, pages 1939-1952) as applied to claims 1, 3, 6, 11, 15-18, 20, 22-30, 37-42 above, and further in view of Ross et al (1997, Molecular And Cellular Biology, vol. 17, pages 2158-2165).

Ross et al teach avian cells have nucleotide binding proteins (see abstract, Material and Methods at page 2159, left column, 3rd paragraph). Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed

invention was made to tranfect avian cells with a polynucleotide for modifying the activity of the nucleotide binding protein with a reasonable expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
December 19, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600